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Mitochondrial dysfunction in cellular senescence

Cellular senescence is a complex biological process characterized by cell cycle arrest and the loss of a cell's ability to divide. Despite the involvement of numerous molecular mechanisms, mitochondria play a central role in this process. Mitochondrial dysfunction, indicated by impaired respiratory capacity and a diminished energy status of the cell, is frequently accompanied by an augmented production of free oxygen radicals, resulting in oxidative stress. This condition not only accelerates cellular aging, but also its progression. A substantial body of research has substantiated the association between mitochondrial dysfunction and cellular senescence, underscoring the significance of mitochondria as a target for anti-aging therapies and interventions. The process of aging is associated with the onset of various age-related diseases, including cancer, cardiovascular diseases, and neurodegenerative diseases. A comprehensive understanding of these mechanisms offers novel opportunities to develop effective strategies that can mitigate the effects of senescence. This article summarizes the mechanisms contributing to the development of mitochondrial dysfunction during aging and discusses the main consequences of this impairment, particularly in the context of its impact on cellular senescence.

Keywords: cellular senescence, mitochondria, oxidative stress, mitophagy, microRNAs, age-associated diseases, cancer, Alzheimer's disease, cardiovascular diseases.

Introduction

Cellular senescence is an inevitable state of cells caused by various stress effects and physiological processes, which is characterized by irreversible cell cycle arrest. The process of senescence is influenced by numerous factors, including the accumulation of DNA damage, the shortening of telomeres, and the deterioration of mitochondria [1]. Senescence cells are known to accumulate in the body, which has been associated with an increased risk of developing multiple chronic diseases, decreased physical stability, and mortality [2]. The precise etiology of aging remains to be elucidated, rendering it a fundamental subject in contemporary scientific inquiry.

Mitochondria are membrane-bound organelles that play a central role in the energy metabolism of cells. They are responsible for a significant part of the production of adenosine triphosphate (ATP) molecules required for various cellular processes. In recent years, mounting evidence has indicated a causal relationship between mitochondrial dysfunction and the major mechanisms of senescence. The process of senescence itself has been demonstrated to be a significant factor in the development of various age-related diseases, including cancer, neurodegenerative diseases, and cardiovascular disease [3]. The exploration of these mechanisms may yield novel strategies for decelerating the aging process and addressing age-related diseases. This review aims to explore the intricate relationship between mitochondria and the senescence process, emphasizing the pivotal role of mitochondria in the development of age-related diseases.

Mitochondria and their role in senescence processes

The efficient operation of mitochondria is vital for the normal functioning of the organism. Mitochondria can be regarded as highly dynamic structures, capable of rapid and substantial adjustment to conditions that reflect the needs of cells. However, it is important to note that various environmental factors, including radiation exposure, as well as endogenous agents, have the capacity to exert influence on mitochondrial function [4, 5]. For example, the synthesis of antioxidants is augmented under conditions of elevated oxidative stress, as well as during periods of enhanced physical exertion, resulting in an escalation of the main mitochondrial enzymes present within skeletal muscle tissues [6]. However, exposure to these factors can lead to mutations in mitochondrial DNA, which in turn contributes to impaired mitochondrial function. Disruption of mitochondrial integrity, both structurally and functionally, is a primary factor contributing to accelerated cellular senescence [4, 7–9].

A plethora of theories has been postulated regarding the etiology of aging. Presently, the free-radical theory of aging, initially proposed by Denham Harman in the mid-1950s [10], occupies a central position among these theories. This theory posits that the accumulation of mitochondrial damage leads to the formation of free radicals, which, when present in excess, can damage cellular components such as proteins, lipids, and nucleic acids.

Mitochondrial DNA (mtDNA) has been shown to be more prone to damage in comparison to nuclear DNA. Its mutagenesis rate has been observed to be 10–20 times higher [11]. This heightened susceptibility can be attributed to the absence of histones and introns within the mtDNA genome, the inefficacy of repair mechanisms, and the proximity to sites of reactive oxygen species formation [12, 13]. It has been established that the frequency of mitochondrial DNA mutations increases with age, and excessive amounts of these mutations can disrupt the normal operation of mitochondria, leading to their dysfunction [14, 15].

Mitochondria are responsible for synthesizing approximately 90 % of the cell's energy, thus acting as the cell's multifunctional energy source. They synthesize ATP in a process known as oxidative phosphorylation via five electron-transport chain complexes. Mutations in mtDNA, which affect genes involved in oxidative phosphorylation, have been shown to have deleterious consequences for cellular energy metabolism, including increased free radical production and decreased antioxidant defenses in the body [16, 17]. Oxidative stress, characterized by an imbalance between the generation and elimination of free radicals, leading to their excessive formation, is considered a contributing factor to cellular senescence. Indeed, research has demonstrated that senescent cells exhibit reduced ATP production efficiency and a diminished energy status [18–20].

Mitochondria, being semi-autonomous organelles, possess a variety of mechanisms that enable them to maintain their integrity under stress. Mitophagy, a term derived from the Greek for “cell death”, is a critical process involved in maintaining a healthy mitochondrial population through the constant destruction of dysfunctional mitochondria [21].

The degradation process is mediated by the autophagosome and was first demonstrated in mammalian cells by electron microscopy [22]. The most studied mitophagy pathway is the Parkin/PINK1-mediated pathway [23]. For example, overexpression of PTEN-induced kinase 1 (PINK-1) in dopaminergic neurons extends lifespan in *Drosophila*, whereas loss of Parkin shortens lifespan [24]. By scavenging dysfunctional mitochondria, mitophagy prevents excessive release of damage-associated molecular patterns (DAMPs), which are based on free-circulating mtDNA [25]. If the damaged mitochondrion cannot be neutralized, mitochondrial membrane rupture and cytosolic release of DAMPs occur, leading to strong inflammatory responses.

Proper control of mitochondrial function can limit inflammation and preserve cell function during senescence, which is supported by numerous experiments [26–28]. In one study, mitophagy also positively affected skeletal muscle cells in mice and humans, preventing senescence [28]. In contrast, disruption of mitophagy contributed to accelerated senescence and the development of several human diseases, including age-related diseases such as Parkinson's disease, Alzheimer's disease [29], cardiovascular disease, and cancer [30, 31].

Mitochondria were originally thought to be isolated organelles, but there is now increasing evidence that they are constantly undergoing fusion and fission. Together, these processes form the basis of mitochondrial dynamics and may also be involved in the control and elimination of dysfunctional mitochondria [32]. The major proteins that enable these processes are mitofusin 1 and mitofusin 2 (Mfn1 and Mfn2) [33]. Mitochondrial fusion can facilitate the exchange of mitochondrial components, including the exchange of mtDNA, which allows the replacement of missing or damaged components in the mitochondrial network [34]. In another case, the mitochondrial proteins Mfn1 and Mfn2 can be degraded, depending on the Parkin-dependent mitophagy pathway, to prevent the fusion of damaged mitochondria with the healthy mitochondrial network [35].

Fission is also a key process in maintaining a healthy mitochondrial population, separating damaged mitochondria from the overall network. Mitochondrial dysfunction disrupts these processes, which can result in a fragmented network dominated by small round or elongated mitochondria [36]. In senescent cells, mitochondria tend to be in a hyper-split state, and deficits in their integrity may contribute to the initiation of various diseases [37, 38], as well as accelerated cellular senescence [39, 40].

In addition to reduced energy status, mitochondrial dysfunction is associated with the development of chronic inflammation [41]. Inflammation is a hallmark of senescence and a risk factor for the development of several diseases, negatively affects the immune system, and accelerates cellular senescence [42, 43]. DAMPs

are the major triggers of inflammation. They are recognized by specialized receptors of the innate immune system, such as toll-like receptors (TLRs) [44, 45]. Activation of this receptor initiates signal transduction pathways that normally trigger inflammation, resulting in the production of pro-inflammatory cytokines, particularly tumor necrosis factor TNF- α and interleukins (IL-6, 8, 12) [46].

Several studies have confirmed a correlation between levels of free circulating mtDNA in cells and proinflammatory cytokines, suggesting a link between mitochondrial dysfunction and inflammatory status [47, 48]. It is now well established that chronic inflammation underlies several age-related diseases such as atherosclerosis, Alzheimer's disease, Parkinson's disease, and type 2 diabetes [49–51].

After reviewing the major functions of mitochondria, we can conclude that they are important regulators of both energy and inflammatory processes, making them key players in the mechanisms of senescence and the pathogenesis of various diseases. As we have seen, genetics plays an important role in controlling and modulating mitochondrial functions. However, in addition to genetics, there is another important aspect that deserves attention — mitochondrial microRNAs.

Mitochondrial microRNAs and their involvement in cellular senescence processes

MicroRNAs (miRNAs) are a group of small non-coding RNAs that play an important role in the regulation of gene expression. The fact that microRNAs are located in mitochondria was discovered only recently, with the first discovery made by Barry and colleagues in 2011 [52]. These molecules have been collectively named “MitomiR”, and each mitochondrion has its own unique set of microRNAs specific to a particular cell type [53]. The origin of these elements may be either the nuclear or mitochondrial genome, and their function is of paramount importance in ensuring proper mitochondrial functionality. They fulfill this role by regulating mitochondrial genes themselves or by modulating the expression of nuclear genes that play a role in mitochondrial processes [54, 55]. In addition, mitochondrial microRNAs can influence mitochondrial dysfunction, making them one of the major catalysts for accelerated cellular senescence [56–58].

Recent studies show that MitomiR serves as crucial sensors of cellular senescence, exerting control over mitochondrial homeostasis and influencing metabolic state, redox balance, apoptosis, mitophagy, all processes closely related to senescence. Some mitochondrial microRNAs, associated with cellular senescence are summarized in the Table.

T a b l e

The role of mitochondrial microRNAs in senescence

Name	Level	Role in senescence	Reference
miR-15b:	↓	Promotes formation of mitochondrial ROS, decreases mitochondrial membrane potential. Causes ATP deficiency, impairing cellular metabolism. Causes the development of a senescence-associated secretory phenotype (SASP), accelerating cellular senescence.	[59]
miR-181c:	↓	Disrupts respiratory complex IV, causing mitochondrial dysfunction. Enhances cellular damage through excessive production of ROS.	[60]
miR-4485:	↑	Negatively modulates respiratory complex I activity, ATP production, increases ROS levels. Inhibits caspase-3/7 activation and apoptosis, slows down mitophagy.	[61]
miR-181a, miR-34a:	↑	Activate Bcl-2, affecting sensitivity to apoptosis, leading to impaired mitophagy, accumulation of old cells. Contribute to mitochondrial dysfunction.	[56]
miR-146a-5p:	↑	Promotes activation of NF- κ B pathway, initiates transcription of pro-inflammatory cytokines. Accelerates senescence through SASPs.	[62]
miR-1, miR-133a, let-7b:	↓	Negatively modulates the function of key proteins involved in oxidative phosphorylation, reduce ETC functionality. Decrease the energy status of the cell.	[62]
miR-378-3p:	↑	Decrease the functionality of ATP synthase. Decrease oxidative capacity.	[62]

Name	Level	Role in senescence	Reference
miR-20b, miR-214, miR-200a-3p:	↑	Negatively affect the expression of MFN1 and MFN2 genes, Disrupt the mitochondrial fusion-release balance, leading to impaired fusion and increased fragmentation.	[63–65]
miR-17:	↓	Promotes ROS formation.	[66]
miR-574-5p:	↑	Regulates protein expression of mitochondrial electron transport chain (ETC) genes, supporting normal mitochondrial function.	[67]
miR-762:	↑	May contribute to inhibition of ATP production and induction of ROS formation and apoptotic cell death.	[68]
miR-106a:	↑	Negatively regulates the expression of some critical cell cycle and apoptosis factors. Inhibits mitophagy.	[66, 69]

Thus, it is easy to speculate that miRNAs can regulate mitochondrial function, and this phenomenon has important implications for the aging process, as mitochondrial dysfunction has devastating consequences for cell fate.

Mitochondrial Dysfunction and Age-Related Diseases

Neurodegenerative diseases

To date, the pathogenesis of neurodegenerative diseases remains in the center of scientific attention as it represents one of the most important problems facing modern society [70]. The factors underlying cognitive impairment in both natural aging and neurodegenerative diseases are not fully understood. There is considerable evidence that mutations in mitochondrial DNA and oxidative stress contribute to accelerated cellular senescence, which is a major risk factor for neurodegenerative diseases.

Alzheimer's disease (AD) is the most common neurodegenerative disease characterized by impairment of memory, language, and other thinking skills, with dementia at its core [70, 71]. A number of mitochondrial abnormalities have been identified in AD: changes in mitochondrial structure, mutations in mtDNA, changes in mitochondrial membrane potential, formation of ROS, decreased ATP, and impaired mitochondrial fusion. There is a wealth of evidence linking mtDNA mutations to the pathogenesis of AD [72–78].

The brain is particularly susceptible to oxidative damage due to its high oxygen consumption. One of the most common defects in the mitochondrial ETC in AD is cytochrome-c-oxidase deficiency, which leads to increased production of ROS and impaired energy metabolism [79]. Several studies have shown impairments of all five ETC complexes in different brain regions in AD [80]. Numerous studies have documented that mitochondrial dysfunction due to abnormal ROS processing is an important factor in the pathogenesis of Alzheimer's disease [81]. It is known that brain cells must constantly produce ATP to maintain neuronal function. For example, oxidative damage to the promoter of the gene encoding a subunit of mitochondrial ATP synthase can lead to a decrease in its level, resulting in decreased ATP production, increased oxidative stress, and cell death [82, 83].

Oxidative stress may also contribute to the pathogenesis of AD by disrupting calcium homeostasis [84, 85]. Glutamate is a neurotransmitter in the mammalian central nervous system that often mediates the synaptic transmission of nerve impulses. However, high levels of glutamate can be toxic, promoting neuronal death [86], and dendritic degeneration [87, 88]. Increased extracellular glutamate leads to its binding to NMDA calcium receptors. NMDA activation causes a massive influx of sodium and calcium into neurons and an outflow of potassium. Elevated Ca^{2+} levels cause irreversible damage to neurons, which promotes neuronal death [89].

Mitochondrial dysfunction and glutamate toxicity are linked. It has been shown that neurons have the ability to “burn” glutamate in the mitochondria, thereby preventing its toxicity [90]. In one of the studies, it was observed that when pyruvate is inhibited in neurons, glutamate consumption by the neurons increases, which leads to a decrease in extracellular glutamate levels, resulting in a decrease in cell death [91]. It is logical to assume that mitochondrial dysfunction will inhibit this process, resulting in an opposite increase in extracellular glutamate levels. Thus, neuroinflammation caused by mitochondrial dysfunction leads to neuronal loss and impaired neuronal plasticity, ultimately leading to Alzheimer's disease. Mitophagy is a critical pathway for mitochondrial quality control. The accumulation of beta-amyloid ($\text{A}\beta$) and phosphorylated tau-protein (pTau) in the brain is a pathological hallmark of Alzheimer's disease. $\text{A}\beta$ and pTau impair mitochondrial integrity and exacerbate mitochondrial dysfunction. Oxidative damage caused by $\text{A}\beta$ and pTau leads to

decreased levels of PINK1 and Parkin protein, which inhibits mitochondrial autophagy and thereby increases A β and pTau [92]. Disruption of fission or fusion processes, namely mutations in the MFN1, MFN2, and OPA1 genes, are also found in several neurodegenerative diseases, including AD [93–96]. In addition, abnormal mitochondrial fission and decreased expression of proteins related to their biogenesis (PGC-1 α , TFAM, and NRF2) have been observed in AD patients, indicating impaired mitochondrial dynamics and biogenesis [97].

Parkinson's disease (PD) is a common neurodegenerative disorder associated with motor dysfunction. A loss-of-function mutation in PARK2 is the most common cause of early-onset PD [98–100]. Loss of function of the PINK1 gene, which encodes a mitochondrial serine/threonine kinase, is the second most common cause of PD [101,102].

Cancer

As early as 1924, Heinrich Warburg discovered that tumor cells are characterized by high glucose consumption and use “aerobic glycolysis” to produce ATP even when oxygen is available. Based on these observations, it has been suggested that altered respiratory capacity caused by mitochondrial abnormalities may be one of the causes of cancer development. Indeed, increased glucose uptake and decreased OXPHOS activity have been observed in many tumor types, and it is believed that high glycolytic capacity is an important hallmark of cancer. For example, glycolysis is common in rapidly growing tumors and oxidative phosphorylation is slowed in these tumors [103].

Oxidative stress due to mitochondrial dysfunction, which is characterized by the production of reactive oxygen species in cells, plays a critical role in cancer development by affecting genome stability and signaling pathways in the cellular microenvironment. Large amounts of ROS, which are by-products of mitochondrial dysfunction, are known to irreversibly damage cellular components, including nucleic acids. Such damage can cause genetic or epigenetic alterations by upregulating oncogenes and tumor suppressor genes. For example, impaired expression of the gene encoding NADH dehydrogenase can stimulate aerobic glycolysis, ROS production, and tumor growth [104].

In addition, ROS can activate various signaling pathways that may contribute to oncogenesis. Examples include the epidermal growth factor receptor EGFR signaling pathway or the Akt/NF- κ B-dependent signaling pathway, which correlate with cancer development [105, 106].

IDH is a family of enzymes involved in oxidative phosphorylation. It includes three isoforms located in the cytoplasm, peroxisomes (IDH1) and mitochondria (IDH2 and IDH3). Some studies show that many tumors, including gliomas and leukemias, have mutations in the genes encoding IDH1 or IDH2 [107, 108].

Cardiovascular Diseases

One of the leading causes of death worldwide is cardiovascular disease (CVD). CVDs are a group of multifactorial diseases that affect the heart or blood vessels. Heart cells have a high energy demand, requiring a constant supply of ATP to maintain cardiac activity. In cardiomyocytes, mitochondria make up about one-third of the cell volume. Not surprisingly, proper mitochondrial function and dynamics are critical for these cells, and their dysfunction is a key factor in cardiovascular disease.

Oxidative stress is central to the development of CVD. Reduced mitochondrial function leads to the production of reactive oxygen species, depletion of cellular ATP, cellular damage and cardiomyocyte apoptosis. Unregulated production of ROS is responsible for a variety of cardiovascular diseases, including cardiac hypertrophy, heart failure, and cardiac ischemia-reperfusion injury [109].

Alterations in mtDNA genes, including NADH dehydrogenase, cytochrome b, and ATP synthase genes, are observed in cardiomyopathies and heart failure [110]. In heart failure, mitochondria are damaged by membrane rupture and depletion of their matrix, resulting in decreased ATP synthesis [111]. It has been shown that patients with heart failure have decreased activity of respiratory complexes I and IV [112]. A study has also shown that the process of mtDNA replication is impaired in cardiomyocytes from people with heart failure, resulting in depletion of mitochondrial DNA, reduction of mitochondrial proteins, and impaired mitochondrial biogenesis [113].

A study has also shown that the process of mtDNA replication is impaired in cardiomyocytes from people with heart failure, resulting in depletion of mitochondrial DNA, reduction of mitochondrial proteins, and impaired mitochondrial biogenesis [114]. Cardiac ischemia due to oxygen deprivation leads to mitochondrial fragmentation due to dysregulation of the Mfn2 protein [115]. The role of mitophagy in the development of CVDs cannot be overlooked. Atherosclerosis is an inflammatory disease of the arteries associated with im-

paired lipid metabolism. The pathogenesis of this disease is associated with the accumulation of macrophages, lipids, cholesterol, migration and proliferation of vascular smooth muscle cells. Mitophagy plays a key role in the removal of these accumulated substances, and disruption of this process will have devastating consequences, increasing vascular plaque formation due to the increase in ROS from damaged mitochondria [116].

Prospects for using mitochondria to fight senescence

Given the close association of mitochondria with senescence, several approaches have been developed and used as strategies to treat mitochondrial dysfunction and age-related diseases. Mitochondrial transplantation is one of the new therapeutic methods used to treat age-related diseases, especially cardiovascular diseases. The essence of the method is the transfer of “healthy” donor mitochondria into cells to replace dysfunctional or damaged mitochondria.

The concept of transferring mitochondria between cells is similar to installing new batteries in malfunctioning devices. By providing healthy mitochondria to cells with impaired energy metabolism, their ability to produce ATP and maintain cell survival can be restored.

One study showed that mesenchymal stem cells could gradually transfer their mitochondria to lung epithelial cells through structures called tunneled nanotubes (TNTs). This transfer helped reduce ATP loss in BEAS-2B cells exposed to cigarette smoke [117]. In another study, umbilical cord mesenchymal stem cells successfully transferred their mitochondria into mtDNA-deficient cells. This restored the expression of genes encoding mitochondrial proteins and improved the function of the ETC [118].

The energy produced by transplanted mitochondria can improve the function of recipient cells. For example, transplantation of isolated mitochondria into ischemic hearts helps to reduce infarct size and improve senolytic function [119]. Mitochondrial transfer opens new doors by providing additional options for the treatment of age-related diseases.

In recent years, hay therapy targeting mitochondria and antioxidants has gained particular popularity. Senotherapy is divided into two groups: senolytics, which kill senescent cells, and senomorphics, which inhibit inflammation. Senolytics have been shown to be highly effective in treating a wide range of age-related diseases, and clinical trials are currently underway for many of these modalities.

Examples of senolytic drugs include BH3 mimetics such as ABT-263 (navitoclax). These drugs are used in certain types of senescent cells based on increased expression of anti-apoptotic proteins of the BCL-2 family [120]. By inhibiting anti-apoptotic proteins, these drugs stabilize mitophagy and thereby remove old cells. In a study, procyanidin, a component of grape seed extract, was shown to have senotherapeutic activity and to extend the lifespan of mice by inhibiting SASP expression [121].

Thus, the use of mitochondria in the fight against aging represents a promising direction that opens new opportunities for improving health and quality of life. The development of various therapeutic approaches aimed at restoring mitochondrial function and overcoming age-related changes may have a significant impact on the treatment of age-related diseases. These strategies highlight the importance of mitochondria as key players in the aging process and their potential role in the future medical approach to longevity.

Conclusion

This article has reviewed the multifunctional role of mitochondria in senescence processes and their impact on cellular physiology. As the major source of cellular energy, mitochondria act as key regulators of oxidative stress in cells. Various environmental factors affect mitochondrial function on a daily basis, leading to an increased frequency of mitochondrial DNA mutations. All of this leads to mitochondrial dysfunction, which in turn causes a decrease in ATP synthesis, production of reactive oxygen species, and promotes chronic inflammation. The vicious cycle between oxidative stress and mitochondrial dysfunction leads to the development of cellular senescence. Furthermore, microRNAs have been demonstrated to play a pivotal role in the regulation of mitochondrial function, which is a critical aspect in comprehending the mechanisms of cellular senescence. A variety of age-related pathologies are marked by distinct mitochondrial mutations, which may contribute to the development and progression of these diseases. Consequently, mitochondria emerge as pivotal subjects for research in the biology of aging and the development of novel therapeutic strategies. A comprehensive understanding of these mechanisms could lead to the development of interventions that enhance health in older individuals and decelerate the senescence process at the cellular level.

Author Contributions

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Жасушаның қартаюы кезіндегі митохондриялық дисфункция

Жасушаның қартаюы — жасушалық циклдің тоқтауымен және жасушаның бөліну қабілетінің жоғалуымен сипатталатын күрделі процесс. Қартаю көптеген молекулалық механизмдерден туындаса да, оның дамуында митохондриялар маңызды орын алады. Тыныс алу қабілетінің бұзылуымен және жасушаның энергетикалық статусының төмендеуімен көрінетін митохондриялық дисфункция жиі тотығу стресіне әкелетін бос оттегі радикалдарының жоғарылауымен бірге жүреді. Бұл жағдай жасушаның қартаюына ықпал етіп қана қоймайды, сонымен қатар оның дамуын тездетеді. Бүгінгі күні митохондриялық дисфункция мен жасушалық қартаю арасындағы байланысты растайтын көптеген зерттеулер бар, бұл митохондриялардың қартаюға қарсы терапия мен араласудың мақсаты ретіндегі маңыздылығын көрсетеді. Қартаю әртүрлі жасқа байланысты аурулар мен жағдайлардың, соның ішінде катерлі ісік, нейродегенеративті аурулар және жүрек-тамыр ауруларының пайда болуымен байланысты. Бұл механизмдерді түсіну қартаюды бәсеңдетуге бағытталған стратегияларды әзірлеу үшін жаңа көзжіектерді ашады. Мақалада қартаю процесінде митохондриялық дисфункцияның дамуына ықпал ететін механизмдер жинақталған, сонымен қатар бұл бұзылыстың негізгі салдары, әсіресе жасушалық қартаюға әсер ету контекстінде қарастырылған.

Кілт сөздер: жасушаның қартаюы, митохондрия, тотығу стресі, митофагия, микроРНК, жасқа байланысты аурулар, катерлі ісік, Альцгеймер ауруы, жүрек-қан тамырлары аурулары.

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Митохондриальная дисфункция при клеточном старении

Клеточное старение — это сложный биологический процесс, который характеризуется остановкой клеточного цикла и утратой способности клеток к делению. Несмотря на участие множества молекулярных механизмов, центральную роль в этом процессе играют митохондрии. Митохондриальная дисфункция, проявляющаяся нарушением дыхательной способности и снижением энергетического статуса клетки, часто сопровождается увеличением продукции свободных радикалов кислорода, что ведет к окислительному стрессу. Это состояние не только способствует клеточному старению, но и ускоряет его прогрессирование. На сегодняшний день существует множество исследований, подтверждающих связь между митохондриальной дисфункцией и клеточным старением, что подчеркивает важность митохондрий как мишени для антивозрастных терапий и вмешательств. Старение связано с возникновением различных возрастных заболеваний и состояний, включая рак, нейродегенеративные и сердечно-сосудистые заболевания. Понимание этих механизмов открывает новые горизонты для разработки стратегий, направленных на замедление старения. В данной статье обобщены механизмы, способствующие развитию митохондриальной дисфункции в процессе старения, а также рассмотрены основные последствия этого нарушения, особенно в контексте влияния на клеточное старение.

Ключевые слова: клеточное старение, митохондрии, окислительный стресс, митофагия, микроРНК, возраст-ассоциированные заболевания, рак, Болезнь Альцгеймера, сердечно-сосудистые заболевания.

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